

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

FRIDAY 11 MAR 2005

To:
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PCT
NOTIFICATION OF TRANSMITTAL OF
INTERNATIONAL PRELIMINARY EXAMINATION
REPORT

(PCT Rule 71.1)

Date of mailing
day/month/year 10 MAR 2005

Applicant's or agent's file reference
12364890/EJH/ar

IMPORTANT NOTIFICATION

International Application No.
PCT/AU2003/001544

International Filing Date
18 November 2003

Priority Date
18 November 2002

Applicant
MURDOCH CHILDRENS RESEARCH INSTITUTE et al

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translations to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide

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PATENT COOPERATION TREATY
PCT
INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 12364890	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. PCT/AU2003/001544	International Filing Date (day/month/year) 18 November 2003	Priority Date (day/month/year) 18 November 2002
International Patent Classification (IPC) or national classification and IPC Int. Cl. ⁷ C12Q 1/68		
Applicant MURDOCH CHILDRENS RESEARCH INSTITUTE et al		

1.	This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2.	This REPORT consists of a total of 5 sheets, including this cover sheet.
	<input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
	These annexes consist of a total of 6 sheet(s).
3.	This report contains indications relating to the following items:
I	<input checked="" type="checkbox"/> Basis of the report
II	<input type="checkbox"/> Priority
III	<input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	<input type="checkbox"/> Lack of unity of invention
V	<input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	<input type="checkbox"/> Certain documents cited
VII	<input type="checkbox"/> Certain defects in the international application
VIII	<input checked="" type="checkbox"/> Certain observations on the international application

Date of submission of the demand 1 June 2004	Date of completion of the report 7 March 2005
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustalia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer ALISTAIR BESTOW Telephone No. (02) 6283 2450

I. Basis of the report

1. With regard to the elements of the international application:*
- ☐ the international application as originally filed.
 - ☒ the description, pages 1 - 95 as originally filed,
pages , filed with the demand,
pages , received on with the letter of
 - ☒ the claims, pages , as originally filed,
pages , as amended (together with any statement) under Article 19,
pages , filed with the demand,
pages 96 - 101 received on 17 December 2004 with the letter of 17 December 2004.
 - ☒ the drawings, pages 1/11 - 11/11 as originally filed,
pages , filed with the demand,
pages , received on with the letter of
 - ☒ the sequence listing part of the description:
pages 1 - 17 as originally filed
pages , filed with the demand
pages , received on with the letter of
2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:
- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
 - ☐ the language of publication of the international application (under Rule 48.3(b)).
 - ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).
3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority in written form.
 - ☐ furnished subsequently to this Authority in computer readable form.
 - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished
4. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/fig.
5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 1 - 20	YES
	Claims 21 - 25	NO
Inventive step (IS)	Claims	YES
	Claims 1 - 25	NO
Industrial applicability (IA)	Claims 1 - 25	YES
	Claims	NO

2. Citations and explanations (Rule 70.7)

The following citations, which were cited in the International Search Report, are relevant for the purposes of novelty and/or inventive step.

- D1. DeRisi J (2000). Unit 22.1: Overview of nucleic acid arrays. In: Current Protocols in Molecular Biology. Supplement 49, pp 22.1.1-22.1.3. John Wiley & Sons, Inc.
- D2. Hone S and Smith R (2002). Otolaryngologic Clinics of North America 35(4): 751-764.
- D3. WO200250305 A1 20 December 2000.
- D4. Dong J et al (2001). Molecular Genetics and Metabolism 73(2): 160-163 (abstract).
- D5. Bacino C et al (1995). Pharmacogenetics 5(3): 165-172 (abstract).
- D6. Kenna M et al (2001). Archives of Otolaryngology — Head & Neck Surgery 127(9): 1037-1042 (abstract).
- D7. Wiszniewski W et al (2001). Genetic Testing 5(2): 147-148 (abstract).
- D8. Pampanos A et al (2002). International Journal of Pediatric Otorhinolaryngology 65(2): 101-108 (abstract).
- D9. Scott D et al (2000). Human Molecular Genetics 9(11): 1709-1715 (abstract).
- D10. Dreyer B et al (2001). American Journal of Human Genetics 69(1): 228-234 (abstract).
- D11. Chen Z-Y and Corey D (2002). Journal of Neurobiology 53: 276-285.
- D12. Database Accession # AC026202. Chen C et al (18 October 2002). Homo sapiens chromosome 3 clone RP11-572B2 map 3p, complete sequence.

Novelty (N) and Inventive Step (IS)

D1 presents an overview of the various uses of nucleic acid arrays, including the use of oligonucleotide arrays for genotyping. D1 does not discuss the genotyping of a subject with respect to connexin 26, pendrin, mitochondrial 12S rRNA or usherin, as specified in the claims. Therefore all of the claims are novel in view of D1. It would not be obvious from D1 to perform the genotyping specified in the claims, and therefore the claims are inventive in view of D1.

D2 presents a review of genetic testing for the evaluation of pediatric hearing loss. This review states that 'screening for mutations in connexin 26 has become increasingly available in many centers and should be performed in all cases of nonsyndromic hearing loss'. In particular, the review cites the role of the connexin 26 mutations 35delG, 167delT and 235delC in genetic screening for deafness. The review also discloses the need for further mutational screening, including in pendrin, for deafness. Such genotyping is so commonly undertaken using oligonucleotide microarray technology that such a method is considered inherent to the disclosure of the citation. D2 does not specify the particular hybridisation conditions referred to in the claims, or the particular oligonucleotides of claims 21 - 25 and therefore the claims are novel. However, there is nothing inventive in the hybridisation conditions specified in the claims, these being very standard in the art.

(continued in Supplemental Box)

VIII: Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Descriptive support

Claims 21-25 are not fully supported by the description. The applicant's invention resides in the provision of methods of genotyping for deafness by immobilized allele-specific oligonucleotide hybridization. In contrast, however, these claims merely recite oligonucleotides *per se*, and do not recite methods for their use in genotyping for deafness. Therefore, in the absence of an inclusion in the claims of methods for the use of these oligonucleotides, the claims are not fully supported by the description.

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of V

Neither has there been shown any inventive merit in using immobilised oligonucleotides SEQ ID 1 - 64 to perform the genotyping, or the sequences themselves, so whilst these may not have been specifically disclosed in D2, their use is not inventive in view of D2. Therefore none of the claims are inventive in view of D2.

D3 discloses the use of immobilized oligonucleotide microarrays for genotyping the connexin 26 35delG mutation associated with deafness. For similar reasons as provided for D2 above, none of the claims show any inventive merit in view of D3.

D4 and D5 (amongst other citations in this field of work) each disclose the use of allele-specific oligonucleotide hybridization for the genotyping of deafness. In particular, these citations disclose the identification of the connexin 26 167delT and 35delG mutations (D2) and the mitochondrial 12S rRNA A1555G mutation. These mutations are specifically detected by the oligonucleotides of the claims. For similar reasons as provided for D2 above, none of the claims show any inventive merit in view of D3.

D6 - D10 each disclose allelic mutations associated with deafness. In particular, these citations disclose the connexin 26 mutations 35delG (D5-D7), M34T (D5, D6), L90P (D5, D7), 167delT (D5), V37I (D5), R143W (D5), 313del14 (D6) and W24X (D7), the pendrin mutations L236P, T416P and E384S (all D8) and the usherin mutation 2299delG (D9). These citations do not disclose methods for genotyping based upon analysis of these mutations, or the specific conditions of hybridisation noted in the claims, and therefore claims 1 - 20 are considered to be novel in the light of these citations. However, these citations disclose the oligonucleotides of claims 21 - 25, and therefore these claims lack novelty. For similar reasons as provided for D2 above, none of the claims show any inventive merit in view of D3.

Furthermore, the consideration of either D1, D2, D3 or D11 in conjunction with any one of D4 - D10 would lead the skilled addressee to the subject matter of the claims, namely the use of specific mutations for genotyping for deafness using immobilized oligonucleotide arrays, and therefore the claims lack inventive step in the light of these combinations of documents.

D12 provides no suggestion as to use or selection of subsequences suitable for genotyping use, and therefore the claims are considered inventive in the light of this citation.

Industrial Applicability (IA)

Claims 1 - 25 meet the requirements of the PCT with regard to Industrial Applicability.